SUPPORT FOR THE AMENDMENTS

Support for the amendment of Claim 16 is found on page 1, lines 8-10 and page 4, lines 20-27, and page 5, lines 9-21, in the specification.

Support for the amendment of Claim 17 is found on page 5, line 24, in the specification.

Support for the amendment of Claim 20 is found on page 2, lines 24-32, and page 5, lines 16-17, in the specification.

Support for the amendment of Claim 21 is found on page 2, lines 33-37, and page 5, lines 19-21, in the specification.

Support for the amendment of Claim 22 is found on page 8, line 31, in the specification.

Claim 25 is amended to delete recitation of "cosmetic active agents" and to add allantoin (page 6, line 37).

Claim 29 is amended to delete the terms "immunosuppressant product" and antiproliferative agent."

Claim 31 is canceled.

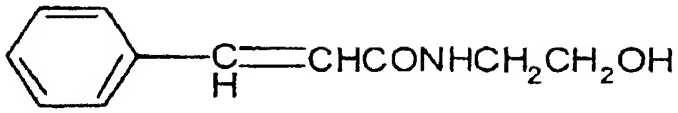
No new matter is believed added to this application by entry of this amendment.

Upon entry of this amendment, Claims 1-17 and 20-30 are active. Claims 1-15 are withdrawn.

REMARKS/ARGUMENTS

The invention according to Claim 16 provides a method for treating rosacea, comprising: topically applying to skin areas exhibiting signs of inflammatory dermatitis associated with any of stages 1 to 4 of rosacea of individuals having fair or sensitive skin, a pharmaceutical composition comprising an effective amount of idrocilamide.

The chemical structure of idrocilamide is:



The chemical name of idrocilamide is N-(2-hydroxyethyl)cinnamide. Applicants have described rosacea (page 1, lines 8-15) as well as the four stages associated with the disease, beginning on page 2, line 8, of the specification.

Applicants respectfully note that Claim 16 is herein amended to recite that the pharmaceutical composition comprising an effective amount of idrocilamide is topically applied to skin areas exhibiting signs of inflammatory dermatitis associated with any of stages 1 to 4 of rosacea of individuals having fair or sensitive skin. This amendment is fully supported in the specification as described in the Support for the Amendments section of this paper.

The rejection of Claims 16-31 under 35 U.S.C. 103(a) over Arkin et al. (WO 02/074290)(Arkin) in view of Barnwarth et al. (Tissue and systemic diffusion of idrocilamide after cutaneous administration) is respectfully traversed.

Arkin describes a topical preparation for treatment of rosacea which contains a non-steroidal anti-inflammatory drug (NSAIDs). NSAIDs are classified according to chemical structure (page 4, lines 5-15) as follows:

> - Salicylic acid derivatives (e.g., aspirin, sodium salicylate, choline magnesium trislicylate, diflunisal, salicylsalicyclic acid, sulfasalazine, olsalazine)
> - Para-aminophenol derivatives (e.g., acetaminophen)
> - Indole and indole acetic acids (e.g., indomethacin, sulindac, etodolac)
> - Aryl acetic acids (e.g., tolmetin, diclofenac, ketorolac)
> - Arylpropionic acids (e.g., ibuprofen, naproxen, flubiprofen,ketoprofen, fenoprofen, oxaprozin)
> - Anthranilic acids (fenamates) (e.g. mefanamic acid, meclofenamic acid);
> - Enolic acids (e.g., oxicams (piroxicam, tenoxicam), pyrazolidinediones (phenylbutazone, oxyphenthratazone)
> - Alkanones (e.g., nabumetone).

Arkin does not expressly teach idrocilamide and none of the structures listed by Arkin are of the cinnamide type structure as indicated above for idrocilamide. Arkin discloses useful examples of NSAIDs on page 4, last 5 lines and none of these examples are of the cinnamide-type chemical structure.

The descriptive term non-steroidal anti-inflammatory drug or NSAID is a broad generic term which classifies structures according to a negative description, i.e., structures that are not a steroid or steroid derivative. Such description encompasses a very large number of known compounds and would include new molecules which prevent the in vivo synthesis of prostaglandins and are nonsteroidal in structure.

The Office acknowledges that Arkin does not expressly teach the inclusion of idrocilamide (Official Action dated August 4, 2011, page 13, line 19) and cites Bannwarth as showing idrocilamide as an effective analgesic and anti-inflammatory agent.

Bannwarth describes a study of the tissue and systemic distribution of idrocilamide in patients suffering from chronic arthropathy of the knee (page 2, lines 8-10; English translation). Bannwarth indicates that motivation for the study was based on the known use of idrocilamide ointment in functional rehabilitation massages and treatment of painful contractures (page 2, lines 1-3). In his study Bannwarth describes that idrocilamide crosses the normal skin coat (page 7, lines 2-4) and moves to the joint capsule and synovial membrane (page 7, line 15). Bannwarth indicates that as a result of his study, a positive relationship could be established between the variation in intensity of pain on the one hand and the respective **concentrations in the muscle, tendon, capsule or synovial membrane** on the other hand. Bannwarth is not directed to effects of the idrocilamide in the dermal layer and does not describe concentration in the dermal layer (see Table 1, page 5).

The Office alleges that (Official Action dated August 4, 2011, page 14, lines 7-10):

> It would have been obvious to one of skill in the art at the time of the invention to include idrocilamide in the invention of Arkin, as motivated by Bannwarth, as Bannwarth teaches that idrocilamide is an effective topical NSAID and the general teaching of Arkin is for the topical use of NSAIDs for rosacea.

However, Arkin is directed to topical application of NSAIDs to target treatment of dermatological manifestations of rosacea, i.e. activity in the dermal layer. In contrast, Bannwarth discloses that idrocilamide permeates through the dermal layer and enters to muscle, tendon and joint capsule of the knee. As Arkin is treating a phenomenon of the dermis, this is opposite of the distribution required by Arkin.

Quoting from In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006), the Supreme Court stated in KSR International Co. v. Teleflex Inc., 550 U.S. 398, 418-419 (2007):

> [R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.
>
> . . . . .
>
> [A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. . . . [I]t can be important to identify a reason that would have prompted a person having ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

The Office has not explained why one of ordinary skill, at the time of the present invention would have been motivated by the disclosure of Bannwarth related to pain relief in the components of a knee joint, to modify the disclosure of Arkin which is directed to treatment of a dermatological disease. Therefore, the Office has not met the burden necessary to support a conclusion of obviousness and withdrawal of the rejection of Claims 16-31 under 35 U.S.C. 103(a) over Arkin in view of Bannwarth is respectfully requested.

The rejections of Claims 25 and 31 under 35 U.S.C. 112, first paragraph and second paragraph, are moot in view of the deletion of "cosmetic active agent" from Claim 25 and the cancellation of Claim 31 herein.

The second rejections of Claims 25 and 31 under 35 U.S.C. 112, first paragraph and second paragraph, are believed obviated by appropriate amendment, herein. Claim 25 is amended to delete the term "skin calmative and protective agents" and to add allantoin. Accordingly, withdrawal of the rejections is respectfully requested.

The third rejections of Claims 25 and 31 under 35 U.S.C. 112, first paragraph and second paragraph, are respectfully traversed.

Applicants note the M.P.E.P. § 2163 II. 2. states:

> Information which is well known in the art need not be described in detail in the specification. See e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)

Applicants note that there is no requirement that "known in the art" does not require that references showing the term in question be related to the present application. "Known in the art" relates to information from any source which is generally available to one of ordinary skill in the relevant art.

As indicated in the references listed in the IDS submitted with this Amendment, propenetrating agents are conventionally known. As indicated in the background description sections of both US 2005/0181999 and US 2009/0104132, propenetrating agents were known at the time of the invention. Examples described in the documents include urea, organic acids, glycols and ethoxydiglycols. Applicants again respectfully submit that these terms are known in the art and that one of ordinary skill would recognize the meaning and substance of Applicants description.

Applicants also again point to U.S. 7,316,810, Col. 4, lines 45-52, which describes propenetrating agents as follows:

> The propenetrating agent, which makes it possible to facilitate the penetration of the active principles, preferably dissolves the active principle present in the composition according to the invention. More particularly, it is chosen from volatile $C_1 - C_4$ alcohols, such as ethanol or isopropanol, from polyhydric alcohols, such as propylene glycol, and from glycol ethers such as ethoxydiglycol.

Finally, Applicants respectfully point to MPEP § 2163 II. 2. which provides the following guidance:

> The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed.

Applicants submit that as described above, one of skill in the art would recognize the present claim element to be implicit to the description of the specification and thus the description "pro-penetrating agent" is fully compliant with the written description requirement of 35 U.S.C. § 112, first paragraph, and provides definitive description to inform one of ordinary skill of the metes and bounds of the invention. Accordingly, Applicants respectfully request that the rejections of Claim 25 under 35 U.S.C. 112, first paragraph and second paragraph, be withdrawn.

The rejections of Claim 29 under 35 U.S.C. 112, first paragraph, are moot in view of the amendment of Claim 29 to delete the terms an immunosuppressant product and an antiproliferative agent.

The rejections of Claims 17 and 20-21 under 35 U.S.C. 112, second paragraph and fourth paragraph, are believed obviated by appropriate amendment.

Claim 16 is amended to recite stages 1 to 4 of rosacea and the dependent claims are amended to further recite treatment of specific stages from 1 to 4. Withdrawal of the rejections is respectfully requested.

The rejection of Claim 27 under 35 U.S.C. 112, second paragraph is moot in view of the deletion of the cited element language in the Amendment filed January 28, 2010. The language is not in the claim.

Applicants respectfully submit that the above-identified application is now in condition for allowance and early notice of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, L.L.P.

Jay E. Rowe, Jr., Ph.D.
Registration No. 58,948

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 07/09)